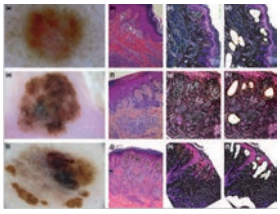
Mutational status of naevus-associated melanomas



This study explores the mutational status of naevus-associated melanomas. The aim was to evaluate the presence of mutations in genes from well-known melanomagenesis pathways in a large series of naevus-associated melanomas. Sixty-one melanomas found in association with a pre-existing naevus were microdissected, after careful selection of cell subpopulations, and were submitted to Sanger sequencing of the BRAF, NRAS, KIT, PPP6C, STK19 and RAC1 genes. Each gene was evaluated twice in all samples by sequencing; by sequencing and another confirmation method, allele-specific fluorescent polymerase chain reaction and capillary electrophoresis detection; or by SNaPshot analysis. Only mutations confirmed via two different molecular methods or twice by sequencing were considered positive. The majority of cases studied presented concordance of mutational status between melanoma and the associated naevus for all six genes (40 of 60; 67%). Nine cases presented concomitant BRAF and NRAS mutations, including one case in which both the melanoma and the adjacent naevus harboured V600E and Q61K double mutations. In two cases, both the melanoma and the associated naevus located on acral sites were BRAF mutated, including an acral lentiginous melanoma. The authors claim this to be the largest naevus-associated melanoma series evaluated molecularly. They report that the majority of melanomas and adjacent naevi studied shared the same mutational profile, corroborating the theory that the adjacent naevus and melanoma are clonally related and that the melanoma originated within a naevus. *Br J Dermatol* 2015; 173: 671-680: 10.1111/bjd.13829

A prospective qualitative study on discharge decision making

This study concerns outpatient discharge decision-making in dermatology. The authors aimed to identify the influences on clinicians' thought processes when making discharge decisions in dermatology outpatients. To do this they interviewed 40 clinicians from 11 National Health Service trusts in England. The interviews were audio recorded, transcribed, coded and thematically analysed. The clinicians' mean age was 48.8 years (range 33–67), 17 (43%) were male and 19 (48%) had >20 years' clinical experience. Overall 148 influences were reported, with five main themes. Disease-based influences included the type of diagnosis (mentioned by 100% of clinicians), guidelines (100%), and treatment needed (100%). Clinician-based influences were the clinician's level of experience (100%), seniority (38%), emotional attitude (95%), 'gut feeling' (25%), personal attitude towards discharge (45%) and level of perception (100%). Patient-based influences included patients' ability to cope with their disease (100%), wishes (70%), quality of life (32%), command of English (40%) and cultural background (25%). Practice-based influences included good primary care (100%), secondary support structure (100%), and clinic capacity pressure (68%). Policy-based influences included pressure from hospital managers (58%) and an active discharge policy (8%). Fourteen influences (9%) were potentially inappropriate. The authors of this study report multiple factors that influence outpatient discharge decision making. They conclude that this now provides the basis to develop evidence-based training to improve discharge decision appropriateness. *Br J Dermatol* 2015; 173: 720-730: doi: 10.1111/bjd.13946

Rapid, reliable, cost-effective molecular diagnosis of epidermolysis bullosa

The extreme clinical and genetic heterogeneity of epidermolysis bullosa (EB) means that labour-intensive and expensive tests are required to establish the correct diagnosis. The investigators aimed to develop a customized, cost-efective amplicon panel for the complete and accurate sequencing of all the pathogenic genes already identified in EB. Additionally, they aimed to minimize the processing time required for the execution of the test and to refine the analytical pipeline to achieve cost-effective results from the perspective of a routine laboratory set-up. The investigators used next-generation sequencing (NGS) via the parallel ultradeep sequencing of many genes as a method for reducing the processing time and costs of EB diagnostics. A panel of EB disease-comprehensive genes in AmpliSeq was established for NGS on an Ion Torrent Personal Genome Machine platform. The panel was performed on 10 patients with known genetic diagnoses and was then employed in eight family trios with unknown molecular footprints. The panel was successful in finding the causative mutations in all 10 patients with known mutations, fully confirming the Sanger sequencing data and providing proof of concept of the sensitivity, specificity and accuracy of this procedure. In addition to the panel being consistent with the clinical diagnosis, they reported that it was also effective in the trios, identifying all of the variants, including ones that the Sanger sequencing missed or *de novo* mutations. The authors concluded that NGS and AmpliSeq made an effective approach for the diagnosis of EB, resulting in a cost- and time-effective 72-h procedure. *Br J Dermatol* 2015; 173: 731-738: doi: 10.1111/bjd.13858